A Start-Up Business Plan as a Scholarly Project

Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School

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Scholarly Report Title: Astraeus Technologies Business Plan

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Collaborators, with Affiliations:

Joe Azzarelli – MIT
Alex Blair – Harvard Medical School
Jay Kumar – Harvard Medical School, Harvard Business School

Description of Team Member Contributions for the Astraeus Technologies Business Plan

Astraeus Technologies consisted of four founding team members, as described in the "Team" section of the business plan. We each contributed to the company in varying ways and took ownership over different aspects of research and development depending on the interests and strengths we each had. We each contributed to developing long-term visions and goals of the company, writing(s) of business plan competitions, and pitching the company to judging panels and potential investors.

I was responsible for market analysis, competitor analysis, identifying and analyzing the regulatory pathway(s) of such a device as the L-CARD, and all graphics/design in the company. I also incorporated the company, took care of all legal and financial aspects of operating the company, and was responsible for bringing in five members of our advisory board. In terms of work time, I spent at least 2,000 hours working on Astraeus in 2015 and 2016.

Jay Kumar was responsible for the financial analysis, developing budgets and projections, and analyzing go-to-market strategies and cost structures. He also took a primary role in courting potential investors and optimizing our business plan competition strategy. He additionally took point on finalizing business plan competitions and generating/editing slide decks.

Alex Blair was responsible for analyzing the clinical foundation of lung cancer screening, the potential utility of the L-CARD, and strategies for how the L-CARD would best fit into clinical practice of different practitioners. He also performed much of the analysis of research literature behind lung cancer screening and clinical practice.

Joe Azzarelli was responsible predominantly for technological/scientific development of the L-CARD itself as well as interfacing with the MIT technology transfer office regarding intellectual property.

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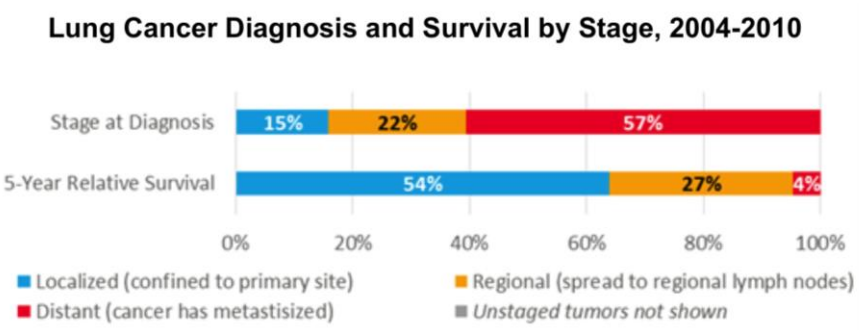
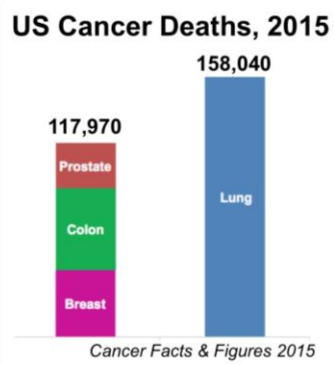
ABSTRACT

Lung cancer is the leading cancer killer, greater than the following three leading causes of cancer combined (prostate, breast, and colorectal). Ninety four million Americans are currently at risk for lung cancer.[1] However, it is only medically and financially advisable to screen the highest risk patients given current screening methods. Screening CTs cost almost eight hundred US dollars each, expose patients to harmful radiation, have a 96% false positive rate, and require expert training for analysis. And while nine million are eligible for such screening, only 1.6 million are conducted in United States each year, which is 1.6% of total at risk Americans. Given this, it is no surprise that only 15% of lung cancers are diagnosed at a localized stage (before lymph node spread and/or metastasis) and only 40% are eligible for surgery. Over half of patients diagnosed with lung cancer die within one year of diagnosis. Even in a restricted patient population, screening all eligible U.S. patients would lead to almost three million unnecessary, harmful, and expensive follow-up studies due to the high false positive rate. These false positives billion U.S. dollars spent annually on unnecessary follow up exams.[2]





More effective lung cancer screening thus has the potential to create medical and economic value. Our solution is a simple, inexpensive gas sensor. Individuals with lung cancer exhale unique gaseous volatile organic compounds (VOCs) at concentrations that people without lung cancer do not. Our device, a Chemically Actuated Resonant Device (CARD), can detect these gases and send diagnostic data to a smartphone. The sensor is a modified near field communication (NFC) tag, a type of Radio-frequency identification (RFID). To create a CARD, an NFC tag is customized with a nanotube-based composite that is activated by specific VOCs. The CARD then wirelessly transfers chemical diagnostic information to a smartphone, which comes with a built-in NFC reader as an industry standard. An L-CARD, a CARD designed for detecting and measuring VOCs related to lung cancer, can be built for one dollar and can be designed to detect a VOC profile with a much greater sensitivity and specificity than screening CT scans.

We would sell L-CARDs directly to hospitals, clinics, and physician practices. Physicians and other health care workers would have control over administering an L-CARD to a patient. Unlike CT scans, L-CARDs can be administered in an exam room or at home and provide diagnostic data immediately via a smartphone. Payors (such as Medicare, Medicaid, or private insurance companies) would reimburse for each L-CARD used.

Looking ahead, CARD-based diagnostics can act as an entirely new medical technology platform. A growing body of research has recently found unique gases in the breath of patients with many different diseases, including breast, colon, prostate, and bladder cancer, as well as malaria, tuberculosis, and pneumonia. Our vision is to adapt our CARD technology to detect the unique gas profiles for other diseases, creating low-cost, highly accurate, noninvasive diagnostic tests for several serious cancers, and in the process establish a company that defines the rapidly evolving market of low-barrier disease screening.

COMPANY OVERVIEW

Astraeus Technologies aims to transform lung cancer diagnosis. Lung cancer is the leading cause of cancer death worldwide. With over 150,000 lung cancer deaths in the United States annually, more than one in four cancer deaths is due to lung cancer. In fact, more Americans die of lung cancer than from the other three leading causes of cancer deaths (prostate, colon, and breast) combined.

Lung cancer is exceptionally difficult to treat and cure due to a variety of factors, most notably because it progresses rapidly and it is difficult to diagnose early. Using current screening guidelines, over 60% of lung cancers are diagnosed at an incurable stage and 79% after they have spread to lymph nodes or metastasized.[3] Over half of patients die within the first year of diagnosis. If lung cancers were diagnosed earlier, treatment would be far more successful in offering patients a cure.

A key barrier to lung cancer treatment is the current screening paradigm, which is incredibly inefficient. The current U.S. standard is annual low dose chest computed tomography (CT) scans for high risk patients. These screening exams have only been recommended since late 2013, but their high price and incredibly high false positive rate means that they are only cost-effective when used in the very high-risk patients. As a result, less than 10% of patients who are at risk for lung cancer are eligible for lung cancer screening. CT scans are expensive, uncomfortable, and harmful, features that limit widespread adoption, despite clinical recommendations. As a result, only 20% of eligible patients are screened in a given year.

Astraeus Technologies will revolutionize the lung cancer screening process. Its patent-protected device, the L-CARD, is a single-use disposable gas sensor that can detect gases in the breath of lung cancer patients and then transmits diagnostic data to a smartphone. Instead of needing to book a CT scan, endure the physical and psychological stress of the exam, subsequently wait for results, and take on the risk of a false positive result, patients would simply blow on an L-CARD in the doctor's office during their annual exam. Physicians would receive highly accurate results immediately through the smartphone and be able to disseminate the information to the patient at the point-of-care. Furthermore, the device is very simple in concept and user friendly, so physicians would require minimal education and training to use it.

The L-CARD is extremely inexpensive to manufacture, has a 5% greater sensitivity, and over twenty times the specificity for lung cancer detection relative to a screening CT scan. Coupled with extreme ease of use, Astraeus Technologies expects that the L-CARD will not only improve screening safety, accuracy, and convenience for the currently eligible population, but also expand screening coverage to a much larger percentage of the 94 million at-risk patients.

TEAM

Founding Team

Astraeus Technologies is comprised of a team of visionary co-founders, strategic advisors, and board members who bring diverse backgrounds to bear on the exciting challenge of bringing breath-based disease diagnostics to the market. Our co-founders Joseph Azzarelli, Alexander Blair, Jay Kumar, and Graham Lieberman are each in their final years of graduate work at MIT, HMS, HBS, and HBS respectively.

Joseph Azzarelli is a chemistry Ph.D. candidate finishing this year at MIT, and is the inventor and lead author on the publication that originally described the CARD, as well as co-author on both of Astraeus Technologies' patents. He has deep knowledge of the state of the art of ultra-trace chemical detection with nanotechnological approaches. Additionally, during the course of his graduate work, he has played a direct role in translating a separate

but related suite of chemical sensing technologies out of the lab and into real world applications, specifically in the food and agriculture sector (C2Sense), as well as in a supporting role in United States defense efforts to develop functional explosive and chemical warfare agent detection technologies (ongoing). In addition to his work in developing first-in-class passive RFID chemical sensing technologies, he has also led undergraduate teams to incorporate chemical sensors into drones, Bluetooth low energy (BLE) devices, and long range (>100 yards) active RFID architectures.

Alexander Blair is finishing his MD at Harvard Medical School and received a master's in health care policy at Carnegie Mellon. He has experience within the technology and policy sphere having worked in Washington DC prior to medical school for HIMSS, a health IT non-profit. His work focused on the policy changes surrounding health IT implementation and reimbursement through the HITECH Act and meaningful use regulations. Additionally, he has worked in medical school on surgical safety checklist implementation, mesothelioma referral guidelines, and health care reform organizations. He has also guided the efforts of a smartphone application that communicates heart attack and stroke risk to patients. He plans to pursue a career in thoracic surgery with a passion for improving lung cancer care. His research includes different surgical approaches for lung cancer removal in the elderly, assist devices for transplantation, and post- operative recovery management.

Jay Kumar is an MD/MBA candidate at Harvard Medical School and Harvard Business School, having completed a Bachelor's in Medical Sciences at the University of Oklahoma where he graduated as the #1 senior male. He invented and co-founded mobile application startup facilitating provider-driven quality improvement in clinical settings. Jay has multiple years of experience in commercializing university intellectual property, business strategy, and medical device startups. As a medical student, he co-founded and served as the co-Editor-in-Chief of the *Harvard Medical Student Review*, and student-run peer reviewed academic journal. He has designed and published several studies in the medical literature on topics including genetic underpinning of disease, healthcare policy and delivery, and surgical techniques and findings.

Graham Lieberman is also an MD/MBA candidate at Harvard Medical School and Harvard Business School. He is a human evolutionary biologist, having trained at Harvard College, with a specific focus in evolutionary orthopedics and skeletal biomechanics. His undergraduate research was centered on load-bearing and transport in human locomotion. He has worked in radiologic education for over ten years. Five years ago, he co-founded and co-authored a web- and mobile-enabled radiological education company that is part of the core curricula at Harvard Medical School and numerous other medical institutions across the country. His company's materials are utilized in over 40 countries worldwide. His professional interests include pediatrics and orthopedic surgery. He is ideally suited as a member of this team as he brings a background in both medicine and business. His first company exists within the digital realm of radiology, and the proposed Astraeus device is a digital diagnostic that would replace a radiologic study. His undergraduate thesis additionally has provided him with a foundation in engineering and machining, skills he would bring to the design and development of the physical apparatus of the diagnostic device.

As four multi-faceted and agile co-founders, we are well poised to lead and grow Astraeus through its inception and into a value-rich entity poised to utilize growth capital. In the near term, we will need to identify and onboard additional strategic advisors, specifically those with expertise in navigating the medical device regulatory environment and payor-hospital nexus.

Programming Team

We have compiled a team of computer scientists with over five years of industry experience to develop the smartphone application for L-CARD signal detection. Eric Wu is the lead computer scientist who graduated from graduated from Carnegie Mellon University with a B.S. in Computer Science and Linguistics. He worked on the mobile games platform team at Amazon, developing parts of its backend and mobile SDKs. After his time at Amazon, Eric joined AQR Capital Management where he helped build out the research platform for the alternative's team. Eric has also worked on a variety of healthcare projects and was a finalist in the Million Hearts Risk Check Challenge.

Advisory Board (**Appendix Figure 1**)

Timothy Swager, John D. MacArthur Professor of Chemistry, MIT: Professor Swager's research interests lie in chemical sensors and electronic materials. He is co-author on the patent behind the L-CARD technology and has been co-founder or advisor in over five tech startups based on research from his lab.

Shantanu Gaur, MD: Dr. Gaur is a gastroenterology resident at Massachusetts General Hospital. A biologist and polymer scientist by training, he has significant experience with medical device start-ups. He is co-founder and COO of Allurion Technologies, a medical device company that has produced a procedure-less gastric balloon for weight loss that was recently approved by the European Medical Agency.

Jon Bloom, MD, MBA: Dr. Bloom is an anesthesiologist, having trained at Massachusetts General Hospital. He is co-founder and CEO of Podimetrics, a medical device company that has produced an FDA-cleared temperature-sensing floormat that can prompt patients to visit a physician before diabetic foot ulcers form. He was the Director of Medical Affairs for Covidien.

Mariya Gusman, MD: Dr. Gusman is a radiology resident at Brooke Army Medical Center and a Captain in the U.S. Air Force. She completed her medical degree at Drexel University and her undergraduate studies in brain and cognitive science at Massachusetts Institute of Technology. She has experience in medical devices and clinical trials.

Ariel Stern, PhD: Dr. Stern is an Assistant Professor of Business Administration in the Technology & Operations Management Unit at Harvard Business School. Her research interests lie in empirical analysis of healthcare markets, healthcare operations, and how regulatory agencies affect innovation in medical technology.

Abraham Lebenthal, MD: Dr. Lebenthal is the Director of Minimally Invasive Thoracic Surgery at the Boston VA Healthcare System and an Instructor in thoracic surgery at Harvard Medical School. He specializes in minimally invasive surgery, particularly as it involves malignant cancers of the lung and esophagus.

Laurie Burlingame, JD: Ms. Burlingame is an Associate at Goodwin Procter's Life Sciences Practice Group. She has significant career experience with both private and public companies in the life science industry, including many medical device and diagnostic companies. Her career focuses lie in company formation, financing, licensing, and corporate governance, among other general corporate matters.

John Silva: Mr. Silva is a co-founder of Tufts Health Ventures and a New Business Developer at Tufts Health Plan. A veteran of the Marine Corps, he has extensive ties to healthcare ventures and startups as well as governmental agencies including CMS, the VA, and DARPA.

Zvi Ladin, PhD: Dr. Ladin is a Co-Founder and Principal at Boston MedTech Advisors with over twenty years of management experience regarding medical devices and regulatory strategy. He received his PhD from the MIT-Harvard Medical School joint Health, Science, and Technology Division and served for five years as a scientific advisor to the FDA.

Additional Expertise

In addition to our programming team and advisors, Astraeus Technology will require additional expertise in legal consultants and intellectual property advising to ensure that we have licensed and patented technology properly. Furthermore, we will consult with regulatory advisors and clinical trial managers to ensure our product is tested properly and has the necessary data to be utilized as a diagnostic device. Finally, we need to consult with or hire a team with manufacturing and distribution expertise when we are at that stage of the product lifecycle.

THE PRODUCT

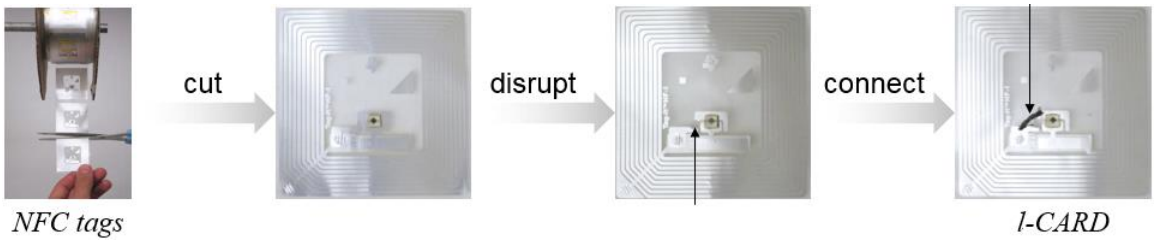
The L-CARD is a breath-based lung cancer screening diagnostic derived from a chemically altered near-field communication tag. Diagnosis is aided by NFC technology intrinsic in industry-grade smartphones that can detect the CARD signal.

Our product is comprised of three components:

. 1) chemically actuated resonance device (CARD)
. 2) disposable receptacle that accepts CARDs
. 3) smartphone application to the CARD-signal derived diagnosis

CARD

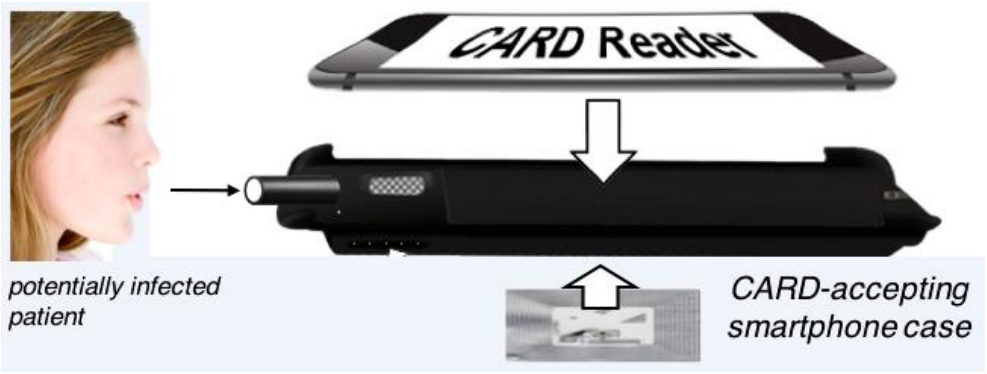
Researchers in the Department of Chemistry at MIT, including a core team member, invented and patented a simple gas sensor: a chemically actuated resonance device (CARD).[4] The sensor is a modified near field communication (NFC) tag with a disrupted circuit. The circuit is reconnected by a nanotube-based composite that can be customized to be activated by specific VOCs in human breath. We aim to adapt the CARD to screen for gases unique to the breath of lung cancer patients (creating an L-CARD[TM]). The device requires minimal raw materials. It is made from NFC tags and micrograms of proprietary composite in two steps: 1) disrupting the RFID tag's circuit with a hole punch and 2) depositing a strip of composite around the hole to reconnect the circuit.[5] The per-unit cost of producing an L-CARD is approximately $1.00 even before the benefits of automation and scale. L-CARDs can be read wirelessly by standard smartphones.



The L-CARD fabrication procedure is simple, reproducible, and scalable.

VOC receptacle

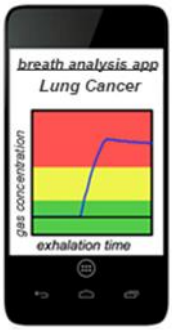
A disposable receptacle will be used to collect a patient's breath sample. This receptacle accepts L-CARDs that are responsive to specific lung cancer VOCs. Upon exposure to lung cancer- specific VOCs, the L-CARD will send a dose-dependent NFC signal that can be detected by a standard smartphone. The receptacle will consist of a one-way valve to ease isolation of patient's breath sample.



The standardized receptacle channels the patient's breath across the L-CARD.

Smartphone application

Our proprietary smartphone application will read activated CARDs and graphically display the concentration of lung cancer-specific VOCs in a breath sample. The application will: 1) recognize NFC tags and match them with specific lung cancer VOCs, 2) analyze the signal intensity and translate this into lung cancer VOC concentration, 3) graphically display VOC concentration, and 4) present lung cancer diagnostic data based on clinically- validated confidence interval ranges.



Our proprietary smartphone app will standardize and simplify screening.

Workflow

We intend for an L-CARD to be used in an outpatient setting in a physician's office. A patient would breathe into a gas receptacle, resulting in an 'activated' L-CARD. The receptacle, containing activated L-CARD would be picked up by a nurse or mailed-in and placed in contact with the office's smartphone with our pre-installed application. The application would then process the L-CARD signal with an NFC antenna and display the concentration of each lung cancer-specific VOC gas. This would then be interpreted by the office physician to establish the diagnosis. The application readout would be isolated from the patient such that our application would not provide the diagnostic data directly to the patient. Interpretation of the diagnostic data and the communication of a diagnosis of lung cancer should be made by a licensed physician. The application display is therefore intended for healthcare professional use only.

Defining features

Our technology improves diagnostic screening for lung cancer on multiple fronts:

Cost: the per-unit cost of producing our technology is <$1, compared to the $795 charge for a CT. Lung cancer patients exhale unique VOCs in biologically relevant concentrations that people without lung cancer do not.[6]

Accuracy: These VOCs have a sensitivity of 94% (vs 88.9% for CT scans)[7] and a specificity of 90% for lung cancer (vs 4.4% for CT scans).[8] By adapting a CARD to detect studied lung cancer VOCs, it has the potential of being highly sensitive and specific. (**Appendix Figure 2)**

Efficiency: They also do not require a technician or radiologist for analysis. The CARD can be shipped in an envelope enabling office-based screening, whereas CT scans and gas chromatography are stationary equipment that require expert analysis.

Safety: The test is non-invasive and does not expose a patient to radiation, unlike CT scans or

potentially harmful follow-up such as biopsy, bronchoscopy, and PET scans.

Consumer fit

There are two main consumers of the L-CARD: patients and healthcare professionals. Patients interact with our technology by blowing into the L-CARD receptacle. In containing a one-way valve, patients will only need to blow directly into the receptacle as VOCs will be contained and exposed to CARDs automatically. This design will minimize loss of VOCs and user variability. Healthcare workers will then handle the L-CARD with a patient's VOC sample and hold it directly against a smartphone with a previously installed Astraeus Technologies application. This application will then display a readout to the healthcare professional with 95% confidence intervals for each lung cancer VOCs.

INTELLECTUAL PROPERTY

Astraeus Technologies' core intellectual property is based on a platform technology invented at and owned by MIT. A license letter-of-intent is in effect. A United States and PCT application have been filed and nationalization will occur in April of 2016. MIT, informed by discussions with Astraeus Technologies, anticipates filing for coverage in the UK, Ireland, Germany, Switzerland, France, Italy, Spain, Portugal, Netherlands, Belgium, Denmark, Sweden, Norway, Japan, South Korea, Australia, New Zealand, Chile, and Argentina.

We surveyed competitive intellectual property first using *Google Patents.* A search of: "'near field communication' 'chemical sensing'" returned 14 results, with our patent as the first returned result. Within this search we identified one patent that ambiguously described a wirelessly coupled blood analysis device, and the remaining patents as being completely orthogonal or irrelevant. Separately, a search of "'chemical sensing' RFID" returned 404 results. Those that were relevant were unanimously described as inventions/ devices that were effectively a conventional chemical analysis platform (e.g. gas chromatography) coupled with an RFID data communication platform. This is not a threat to our IP nor a challenge in terms of freedom to operate as these devices are plug-and-play combinations of existing technologies and are not a fundamentally novel method of chemical information transmission as is characteristic of our technology.

MARKET ANALYSIS AND MARKETING STRATEGY

Market definition

The National Institutes of Health estimate cancer care to cost $124.6 billion in 2010, $12.1 billion of which is due to lung cancer.[9] Lung cancer causes more deaths than colorectal, breast, and prostate cancers combined killing 158,040 Americans in 2015 or 27% of all cancer deaths.[10]

The burden of lung cancer is growing. Approximately 402,000 Americans living today have been diagnosed with lung cancer, but an estimated 221,200 new cases are expected in 2016.[10] Deaths caused by lung cancer increased approximately 3.5% between 1999 and 2012, in greatest proportion for elderly women.[11]

There are 94 million current or former smokers in the United States at elevated risk of developing lung cancer.[12] Unfortunately, current screening capabilities are so poor that only 8-9 million of the highest-risk Americans receive annual low-dose screening chest CT scans.[13] Our product, the L-CARD, will be positioned specifically to replace screening CT scans in those 8-9 million Americans, with the possibility of subsequently expanding to serve the remaining 85 million at risk for lung cancer. Over time, given that lung cancer is so common and that 10-15% of lung cancers are not associated with smoking,[14] it is reasonable to suspect that the L-CARD could become a routine screening test for the general population, much the way mammograms and colonoscopies are now

Currently, only 1.6 million Americans actually receive screening CT scans, meaning approximately 80% of people indicated for screening do not receive it. This likely stems from the negative patient-specific aspects of CT scans, such as being uncomfortable, expensive, and time- consuming. Due to the unpleasant process of undergoing a CT scan, as well as the inaccuracy and delay in diagnosis, patients on average are diagnosed at a later stage of disease than they could be with better screening. This likely explains why only 40% of the 200,000 patients diagnosed with lung cancer in the US yearly are diagnosed at a stage early enough to be curable.

Market size

With the large number of heavy smokers in the country, however, lung cancer screening is an increasingly expensive burden on the healthcare system. Chest CT scans have a median price of $795.[15] If all nine million eligible Americans were screened, that would result in a $7.2B expenditure. However, screening causes additional costs in the follow-up exams it elicits and expensive complications. Twenty-four percent of screening CT scans return a positive result; of those, 73% require additional higher-resolution CTs, 11.3% require a surgical procedure and/or biopsy, and 10% require PET scan.[16] The follow-up surgical procedures and biopsies cost between $1000 and $6000 each[17,18,19] and PET scans cost on average $3,000.[20] This translates to an additional $2.9B expenditure on follow-up exams. However, since 96% of positive screening tests are false positives,[21] the vast majority of follow-up costs could ultimately be avoided if a more specific test (more specific meaning fewer false positives) was developed.

The gases the L-CARD would be designed to detect have a significantly better sensitivity and specificity than screening CT scans currently do. The false positive rate and false negative rate for the gases in question are 5-10% and 6%,[6,8] respectively (vs. 96% and 11%,[7] respectively, for CT scans). This, coupled with a variable cost of approximately $1.00, is our key value proposition to consumers: the L-CARD is a more effective screening test than screening CT scans and costs significantly less to produce on a per-unit basis. This value could reasonably expand our market to the 85 million at-risk for lung cancer not currently eligible for screening with CT scans. The current expense of the gold-standard allows for a hefty range of prices (up to hundreds of dollars, even) that would still be attractive to current consumers. This puts us in a comfortable position to set a price for the L-CARD that would easily cover our sunk costs of development, clinical trials, and costs of production, while still providing attractive margins for Astraeus Technologies management and investors.

Customers

We would sell L-CARDs to hospitals and clinics as a cheaper, safer, and easier screening test than CT scans. Our marketing strategy would focus on four key aspects: 1) efficacy, 2) price, 3) ease of use, and 4) safety.

Efficacy

Lung cancer patients exhale unique VOCs in biologically relevant concentrations that people without lung cancer do not.[22] These VOCs have a sensitivity of 94% (vs 88.9% for CT scans)[7] and a specificity of 93% for lung cancer (vs 4.4% for CT scans)[8,23,24]. By adapting a CARD to detect studied lung cancer VOCs, it has the potential of being highly sensitive and specific.

Price

Given estimates of research and development costs (see Financial section below), L-CARDs are significantly less expensive than CT scans. The per-unit cost of producing our technology is <$1, compared to the $795 charge for a CT. As a result, we would charge $100 per L-CARD. This would provide attractive margins for Astraeus Technologies in production and recoup the cost of research, while

still providing a huge amount of value for payors and providers.

Ease-of-use

L-CARDs are easier to use than CT scans. They are small, portable, and could be bought and shipped in bulk, unlike CT scans. They can be administered in the healthcare worker's exam room at the point of care or used at home, without needing a separate department or facility with separate scheduling like a CT scan, and provide immediate results. All that is required for L- CARD analysis is a patient's breath sample and smartphone. L-CARDs also do not require patients to undergo the discomfort of physically entering the scanner and holding still during the scan. As the L-CARD signal can be displayed by our application, a technician or radiologist is not required for analysis.

Safety

The CARD is non-invasive and does not expose a patient to radiation, unlike current screening practices such as CT scans, PET scans, bronchoscopies, and lung biopsies. Approximately 1 in 2000 CT scans (at 10mSV of radiation) causes a fatal cancer that would not have developed otherwise.[25] Radiation exposure from a single chest CT scan is 2mSV for a low dose[26] and 7mSV for a standard scan.[27] Lung biopsies result in pneumothorax (lung collapse) requiring chest tube and hospital admission for 2-5 days in 7% of cases and bleeding requiring blood transfusion in 0.2% of cases.[28]

Marketing strategy

L-CARDs would likely require buy-in from both healthcare workers and the hospitals that employ them as well as from insurance companies as a whole. The most important barrier to cross before attracting them as customers is adequate data collection. Results of clinical trials and human testing demonstrating the efficacy of the L-CARD is the primary concern; they must be published in the most prestigious peer-reviewed journals as possible. With regulatory backing stemming from these data, the task would be convincing healthcare workers and payors that the L-CARD is a superior alternative to screening CT scans. To more easily speak to healthcare workers and insurance companies, our marketing team will be comprised of individuals with experience in healthcare. Healthcare workers must be willing to use the L-CARD instead of ordering a scan. Once they are willing to do so, they will be willing to speak to hospital or clinic management to add L-CARDs to the list of medical devices/supplies ordered from medical wholesalers. At the same time, insurance companies must be willing to reimburse health care workers for using L-CARDs, which will be dependent on the specific nature of the contract the insurance company has with the healthcare worker's facility regarding the specific patient population in question.

Distribution

The main product requiring distribution is the CARDs. One of the most attractive aspects of CARDs is their low cost and size. Rolls of generic NFC tags can be shipped in rolls of hundredsor even thousands as each one weighs mere grams. The weight of CARDs after they are modified from generic NFC tags are largely the same. CARDs would require individual, airtight packaging to maintain the integrity of the nanocomposite application. As a result, it is unlikely CARDs will be shipped in rolls, but they are still likely to be distributed en masse, with relatively low shipping costs on both a per-unit and bulk basis. As a result, distribution of CARDs could be accomplished in two channels: 1) direct to consumer, in which Astraeus Technologies would ship CARDs directly to consumers, or 2) via medical wholesalers, in which Astraeus Technologies would partner with large distributors to send out regular shipments of CARDs most likely to larger hospitals and academic centers.

The other components of the diagnostic device are the user-interface application and disposable breath-trapping containers. The application can be distributed at effectively no cost, once it is written. It is a piece of software that the end-user would need to download onto their NFC reader-enabled smartphone. The

disposable breath-trapping containers would likely be distributed with individual CARDs on a one-to-one basis through the same distribution channels.

Competitors

Astraeus Technologies has two key competitors: CT scan providers and breath-based sensor companies. The former competitors (e.g. Siemens and GE) have strong market penetration with a product that is the gold standard for lung cancer screening. However, as discussed previously, the CARD technology is superior to CT scans on nearly every dimension. With better accuracy, safety, cost, and efficiency, we expect insurance companies will rapidly adapt our technology after trials directly comparing the efficacy CARDs to CT scans, which we expect to complete within three years. As for the latter competitors, in the past decade, research entities have proposed six different VOC sensors (e.g. colorimetric, carbon-polymer, surface acoustic wave, gold nanoparticle, metalloporphyrins-coated quartz microbalance). Of these sensors, most still remain as research products that are not being commercialized. However, we have identified two potential competitors that are developing sensors from colorimetric and carbon-polymer arrays. Both of these sensors have shortcomings that our technology does not have. Colorimetric "labs-on-a-chip" are simple chemical sensors that change color in response to exposure of a fluid chemical in question. However, reading the result of the test is relatively imprecise, much the way reading a pH test-strip is imprecise.

Carbon-polymer arrays have the advantage of being fairly flexible, able to detect multiple different compounds simultaneously. As such, they work more as an "electronic nose." However, the flexibility of detecting multiple compounds comes at the price of accuracy - electronic noses require a lot of complex, statistical analysis to determine what compound(s) is present in a sample and in what concentration. Additionally, these carbon-polymer arrays are typically rigid, inflexible, and require an on-board power source or electrical connection. The CARD technology is a simple gas-sensor that is designed to detect only one gas in a dose-dependent manner, and to do so with extreme accuracy and precision. It is also flexible (and thus less prone to breakage) and does not require a power source as it is a resonant circuit that "reflects" a signal back from an external source (in this instance, a phone) with no need to generate a signal internally. In these ways, Astraeus Technologies' CARD is more lean, agile, and accurate than our future competitors' technologies. (**Appendix Figure 3**)

The *L-CARD*, a simple RFID-based gas sensor, can bring the hypothetical diagnostic capabilities of GCMS to the clinic in a safe, inexpensive manner. The *L-CARD* is based on technology developed by one of our co-founders within the Department of Chemistry at MIT (please see section III).[29] In the first report on the CARD technology, the authors established semi- quantitative detection limits of VOCs and gases down to 4 parts per million (ppm) (**Appendix Figure 4**).[4] Subsequent work within the same laboratory at MIT has pushed fundamental detection limits to below 10 parts per billion (ppb);[30] this is well below the required biologically relevant detection limits needed in a breath analysis device.

OPERATIONS

Product development (**Appendix Figure 5**)

There are three main components to the diagnostic device, each of which must be developed and tested simultaneously. These components are the mobile application, the breath delivery apparatus, and the CARD itself. As described above, the CARD is the actual chemical sensor that would detect the diagnostic VOCs in question. The breath delivery apparatus is a simple piece of plastic that is designed to standardize the volume of breath exposed to the CARD and the time of exposure. The mobile application is the user interface in the smartphone that interprets the signal generated from the CARD and displays it in a user-friendly graphical interface to provide data for diagnosis and any other relevant information, such as likely

cancer type or staging if possible.

Each of these components will be built successively in stages, initially in a proof of concept, then as a minimum viable product, and then with increasing complexity and clinical utility. The proof of concept product consists simply of a CARD that reacts to acetaldehydes in general and a mobile application that can detect the signal of said CARD in an on/off pattern. We have chosen acetaldehydes as a proof of concept because they are components of numerous compounds found in the medical literature associated with lung cancer. We expect to have a proof of concept product developed by the middle of February, 2016 at a cost of approximately $1,500.

Our minimum viable product will be an extension of our proof of concept. The CARD will detect a single gas that is more specific lung cancer based on our literature review, most likely hexanal. The mobile application will also be more sophisticated and will be able to gauge signal strength, which correlates with gaseous concentration and thus with disease burden. As a result, this iteration of the mobile application means the CARD is no longer a binary sensor (on *vs.* off, or whether the gas is present *vs*. not present) but is actually a dosimeter. This would be useful information to utilize in cancer staging when positive results are obtained. Furthermore, this iteration of the diagnostic would also include a breath delivery apparatus. This apparatus would consist of two separate chambers, one that is initially filled to a set volume of patient's breath. This chamber can be emptied in a mechanically regulated manner to a second chamber that contains the CARD, exposing the CARD to the specified volume of breath for a set period of time. This would standardize the volume and time of gas exposure for the CARD allowing for standardized, replicable results. We expect to create this minimum viable product by July, 2016 at a cost of approximately $20,000.

From there, our next steps in development largely revolve around human trials and refinements therein. At this point, it is unclear whether our final diagnostic device will be effective if it simply detects one gas or will require detection of multiple. There are several gases studied, each of which have high sensitivities and specificities for screenable lung cancers, and it is unclear which gas(es) should be chosen for our device. The CARD, breath delivery apparatus, and mobile application together would require FDA approval (or 510(k) clearance) for human studies to determine the optimal design of the device. We expect that these human trials will take approximately three years to perform. Development of the device in its final form will cost approximately $10M plus an additional $5M for running the clinical trials themselves. All in all, we expect to have a final product ready for approval by 2020.

Clinical trials

Astraeus Technologies will first submit an Investigational Device Exemption (IDE) to allow for the L-CARD to be used in a clinical study in order to collect safety and effectiveness data. We will partner with Dr. Mariya Gusman to conduct our stage I trial at Brooke Army Medical Center. By June 2016, we will submit our proposal to the institutional review board (IRB). Throughout the following three months, we will revise our study proposal as per Brooke Army Medical Center IRB guidelines. The L-CARD will be labeled for investigational use only and we will obtain informed consent for all patients. The clinical trial will run from September 2016 through December 2016 allowing us to collect data for over 500 patients. In order to determine the combination of lung cancer VOCs that yields the highest sensitivity and specificity, we will conduct five trials with 100 patients each, with a different VOC studied in each trial.

Upon completion of the five stage I clinical trials, we will develop an L-CARD 2.0 that detects multiple gases. L-CARD 2.0 will detect lung cancer gases of the highest sensitivity and specificity gases from the stage I clinical trials so as to create an L-CARD with a sensitivity and specificity greater than 95%. We are confident this will be possible as just one of the VOCs that is detectable with our technology, 3-

hydroxy-2-butanone, has a sensitivity of 93.0% and 92.7% using gas chromatography.[23] We will conduct our stage II clinical trial from February 2017 through April 2017 with 1000 patients.

Both trials will be conducted within existing clinical workflow for screening of patients with low dose CT scans using USPSTF guidelines. As screening data will be readily available, including CT scans, biopsies, and further follow-up studies, we will be able to readily determine whether the L-CARD has improved safety and effectiveness as compared to existing screening diagnostics.

FDA approval

We will register the L-CARD as an FDA class II device. All other gas sensing technologies previously approved by the FDA, such as carbon dioxide (Sec. 868.1400) and carbon monoxide (Sec. 868.1430) gas sensors are listed as class II devices. These devices harness technologies such as chemical titration, absorption of infrared radiation, gas chromatography, or mass spectrometry. The L-CARD is a nanotube-based chemiresistor and as such has a dissimilar technological characteristic as compared to these other sensors. However, the L-CARD is arguably substantially equivalent to Sec. 868.1400 and Sec. 868.1430 since it has the same intended use of measuring a gaseous analyte and does not raise new questions of safety and effectiveness. In terms of safety, the L-CARD is a non-invasive diagnostic and, while the CARD is manufactured with potentially carcinogenic solvents, the final L-CARD will not be carcinogenic. As a class II device, we will be exempt from submitting a premarket approval (PMA) application and alternatively will submit a 510(k) application to demonstrate premarket safety and efficacy equivalent to other gas sensing technologies already cleared by the FDA, in accordance with 21 CFR Part 807 Subpart E.

Upon acceptance by the FDA of the 510(k) exemption, we will submit for establishment registration with the FDA as required under 21 CFR Part 807 Subpart B at a current cost of $3845 in 2016. This registration will be submitted on an annual basis henceforth at the rate established by the FDA. We will additionally submit at that time a listing of all medical devices and components of medical devices manufactured by Astraeus Technologies facilities, including but not limited to the L-CARD and the mechanical housing for breath. We will design, produce, and distribute the L-CARD, mechanical housing for breath, and all other medical devices with good manufacturing practices to meet FDA quality system requirements as stipulated in 21 CFR Part 820. The L-CARD system will then be labeled and advertised according to the FDA Federal Food, Drug, and Cosmetic Act (FFDCA) Section 201(k) guidelines when the device is brought to market.

LEGAL AND GOVERNANCE

Astraeus Technologies, Inc. is a for-profit Class C company incorporated in Delaware in November, 2015. The backgrounds of the four co-founders are discussed above in the ‘Founding Team’ section.

Given the early stage of our company, our board of directors currently consists only of Graham Lieberman. We have kept our board of directors as only one individual currently to allow for the agility required in an early stage startup. The four co-founders, however, work together to come to mutually agreed upon decisions before Mr. Lieberman enacts them on behalf of the company as the sole board member.

FINANCIAL SNAPSHOT

After the first 3 years of development and trials, and establishing sales channels and partnerships, we will start earning revenues. We expect to sell 4,000 units in year 4, and grow incrementally for 1-2 years, and then scale up from there. So, we will see our first revenues in year 4, and we will be cash flow positive that year. We achieve breakeven by end of year 5. Please see **Appendix Figures 6 and 7** for detailed financial projections.

CAPITAL REQUIREMENTS

Our immediate capital requirements are $75,000 to fund a small feasibility trial in patients this summer. This will include patient enrollment, raw material and manufacturing costs, and other trial operations.

Our pro-formas assume a total funding need of $2.2MM over the first 3 years. These funds will support additional trial studies, lab space, warehousing, scale in manufacturing, labor, IP protection, and sales.

APPENDIX

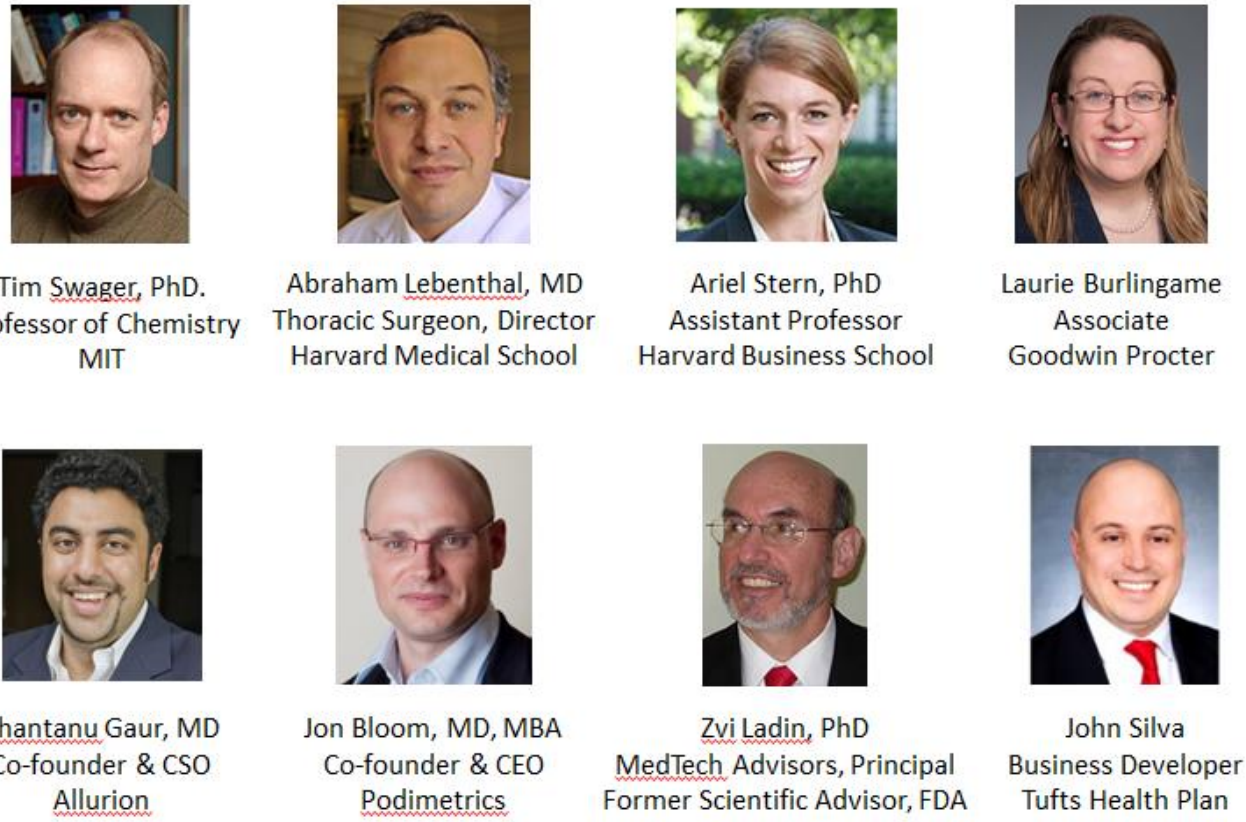


Figure 1. Astraeus Technologies' advisory team.

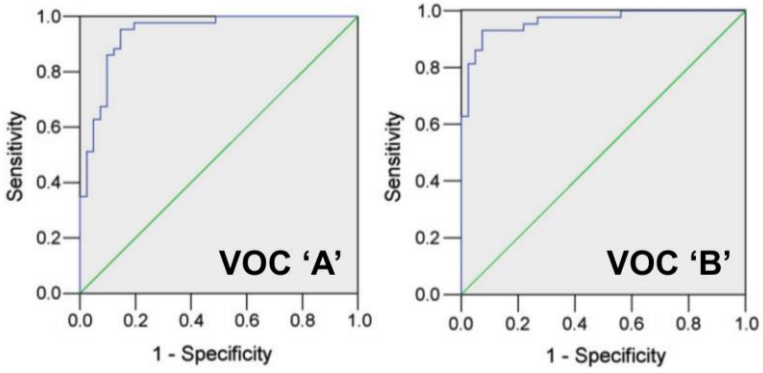


Figure 2. Receiver operating characteristic (ROC) curves for two VOCs indicative of lung cancer. Taken from G. Song et al. (Lung Cancer 67 (2010) 227-231).

	characteristic	optimal	minimal	CT Scan	electronic nose	L-CARD
scope	goal of test	A screening test to: 1. determine if a patient has lung cancer. 2. If the patient has lung cancer, determine the stage of lung cancer.	determine if a patient has lung cancer, at any stage			
	target population	anyone who has ever smoked or been exposed to airborne toxins	adults 55 - 80 with 30 pack year smoking history and currently smoke or have quit within the past 15 years			
	target administer of test	any physician, nurse practitioner, medical technician, or clinician	medical technician			
	lowest setting for implementation	any practice, clinic, or treatment center including 'mobile,' 'walk-in,' and 'commercial' clinics	physicians practice			
performance characteristics	diagnostic sensitivity	96% - 99%	90% - 95%			
	analytical sensitivity	100 part per billion VOC biomarker(s)	1 part per million VOC biomarker(s)			
	diagnostic specificity	96% - 99%	90% - 95%			
	analytical specificity	responds only to desired VOC biomarker(s)	responds only to VOC biomarkers and other non-interfering VOCs			
	quantitation	quantitatively assign stage with 99% confidence interval	quantitatively assign stage with 95% confidence interval			
	reproducibility	always works	works 99% of the time			
	stability	external conditions do not influence diagnostic performance	external conditions influence diagnostic performance minimally			
	interference	diagnostic test is not confounded	diagnostic test is confounded within an acceptable range			
	earliest clinical detection	dysplasia	stage 1 lung cancer			
operational characteristics	patient prep	none	minimal (less than one hour)			
	time to result	<1 hour	<1 day			
	instrumentation	handheld device	dedicated instrument			
	power requirements	wireless, rechargeable	wall-powered			
	maintenance/calibration	none (factory calibrated)	<once per month			
	data analysis	direct comparison to standard value	software- and/or human-analysis			
	connectivity	cellular or bluetooth	wifi or LAN network			
	result capture, documentation, data display	instantaneously interpretable & integrated with patient record	manual upload by medical technician			
	operating temperature/ humidity/ altitude	unaffected	minimally affected			
	storage	storable for 3 years	storable for 6 months			

legend	
	meets optimal requirement
	meets minimal requirement
	does not meet minimal requirement
	not applicable/unknown
	based on literature data

Figure 3. Target product profile analysis.

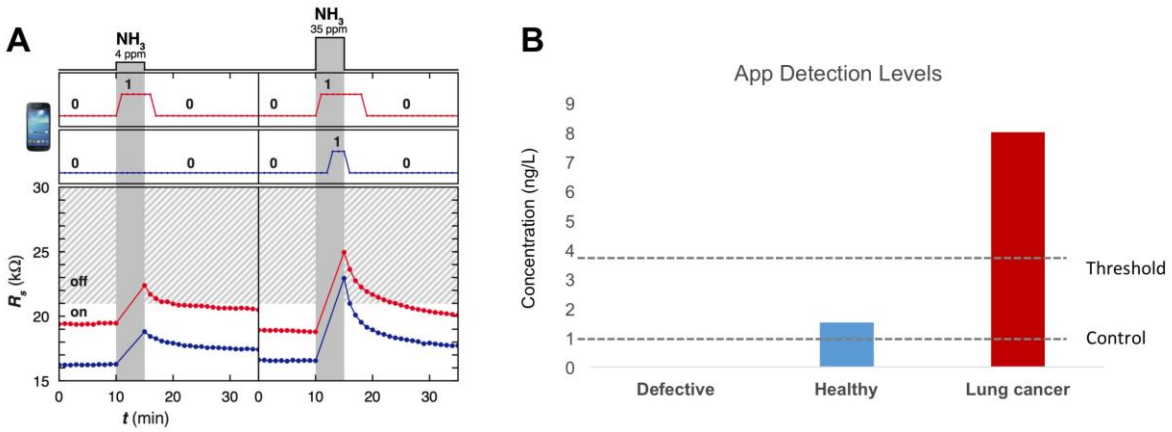


Figure 4. (A) The CARD platform has been shown to reproducibly and semi-quantitatively detect gases at 4 ppm and lower. '0' indicates that the tag is in the 'on' state; '1' indicates that the tag is in the 'off' state, as defined by the signal received by the smartphone. Taken from J. Azzarellli et al. (Proc. Natl. Acad. Sci. 111 (2014) 18162-18166). (B) Architecture of diagnostic recommendation algorithm (gas intentionally left undefined).

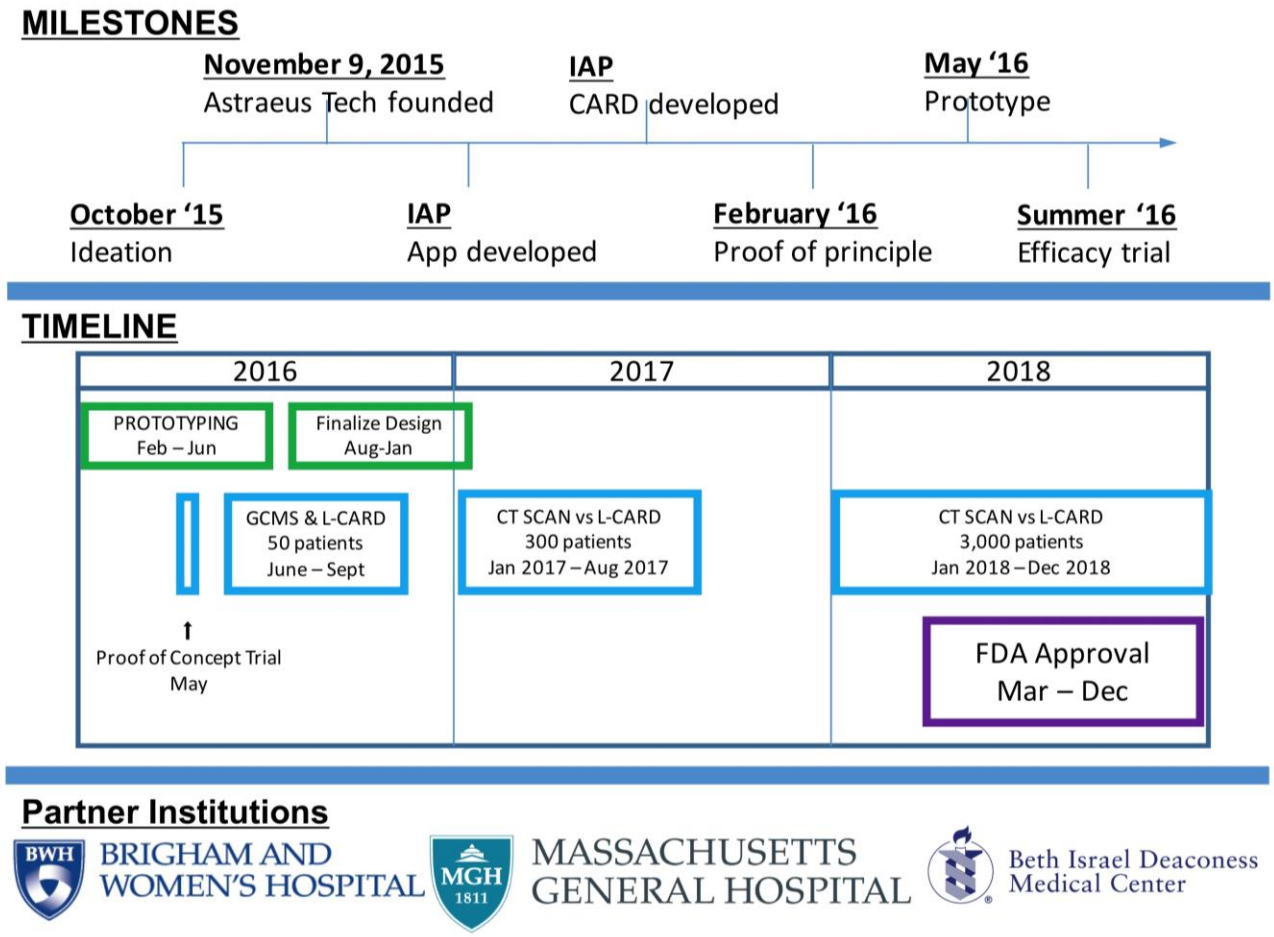


Figure 5. Milestones and projected clinical feasibility development timeline.

Income Statement										
	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
# Units				4,000	8,000	16,000	30,000	50,000	75,000	100,000
Price				$200	$200	$200	$200	$200	$200	$200
Revenue	**$0**	**$0**	**$0**	**$800,000**	**$1,600,000**	**$3,200,000**	**$6,000,000**	**$10,000,000**	**$15,000,000**	**$20,000,000**
YOY Growth %					*100%*	*100%*	*88%*	*67%*	*50%*	*33%*
Raw Material				($2,200)	($4,400)	($8,800)	($16,500)	($27,500)	($41,250)	($55,000)
Manufacturing				($30,000)	($32,500)	($32,500)	($32,500)	($32,500)	($32,500)	($32,500)
Shipping				($1,800)	($3,600)	($7,200)	($13,500)	($22,500)	($33,750)	($45,000)
Gross Profit	**$0**	**$0**	**$0**	**$766,000**	**$1,559,500**	**$3,151,500**	**$5,937,500**	**$9,917,500**	**$14,892,500**	**$19,867,500**
GM%				*96%*	*97%*	*98%*	*99%*	*99%*	*99%*	*99%*
Start-up Costs	($104,120)	($1,097,000)	($600,000)							
IP / Legal	($58,333)	($58,333)	($58,333)	($50,000)	($50,000)	($50,000)	($50,000)	($50,000)	($50,000)	($50,000)
Salaries		($35,000)	($135,000)	($185,000)	($320,000)	($420,000)	($455,000)	($605,000)	($605,000)	($605,000)
Fixed G&A		($15,000)	($15,000)	($90,000)	($105,000)	($110,000)	($110,000)	($115,000)	($120,000)	($125,000)
Operating Income	**($162,453)**	**($1,205,333)**	**($808,333)**	**$441,000**	**$1,084,500**	**$2,571,500**	**$5,322,500**	**$9,147,500**	**$14,117,500**	**$19,087,500**
Margin %				*55%*	*68%*	*80%*	*89%*	*91%*	*94%*	*95%*
Taxes Payable	($56,859)	($421,867)	($282,917)	$154,350	$379,575	$900,025	$1,862,875	$3,201,625	$4,941,125	$6,680,625
+/- NOL	$56,859	$421,867	$282,917	($154,350)	($379,575)	($227,717)	$0	$0	$0	$0
Cash Taxes	$0	$0	$0	$0	$0	$672,308	$1,862,875	$3,201,625	$4,941,125	$6,680,625
Net Income	**($105,595)**	**($783,467)**	**($525,417)**	**$286,650**	**$704,925**	**$1,671,475**	**$3,459,625**	**$5,945,875**	**$9,176,375**	**$12,406,875**
Margin %				*36%*	*44%*	*52%*	*58%*	*59%*	*61%*	*62%*
Balance Sheet										
Cash	$0	$0	$0	$252,384	$1,168,986	$2,728,651	$5,592,228	$10,685,534	$18,795,574	$30,136,113
Accounts Receivable	$0	$0	$0	$131,507	$263,014	$526,027	$986,301	$1,643,836	$2,465,753	$3,287,671
Inventory	$0	$0	$0	$40,000	$80,000	$160,000	$300,000	$500,000	$750,000	$1,000,000
Tax Asset	$56,859	$478,725	$761,642	$607,292	$227,717	$0	$0	$0	$0	$0
PPE	$0	$0	$0	$25,000	$22,500	$20,000	$17,500	$15,000	$12,500	$10,000
Assets	$56,859	$478,725	$761,642	$1,056,182	$1,762,217	$3,434,678	$6,896,029	$12,844,370	$22,023,827	$34,433,784
Accounts Payable	$0	$0	$0	$7,890	$9,000	$9,986	$11,712	$14,178	$17,260	$20,342
Paid-In Capital	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Retained Earnings	($105,595)	($889,061)	($1,414,478)	($1,127,828)	($422,903)	$1,248,572	$4,708,197	$10,654,072	$19,830,447	$32,237,322
Cumulative Funding Need	$162,453	$1,367,787	$2,176,120	$2,176,120	$2,176,120	$2,176,120	$2,176,120	$2,176,120	$2,176,120	$2,176,120
Shareholders Equity	$56,859	$478,725	$761,642	$1,048,292	$1,753,217	$3,424,692	$6,884,317	$12,830,192	$22,006,567	$34,413,442
Liabilities + SE	$56,859	$478,725	$761,642	$1,056,182	$1,762,217	$3,434,678	$6,896,029	$12,844,370	$22,023,827	$34,433,784
Statement of Cash Flows										
Net Income	($105,595)	($783,467)	($525,417)	$286,650	$704,925	$1,671,475	$3,459,625	$5,945,875	$9,176,375	$12,406,875
Depreciation	$0	$0	$0	$0	$2,500	$2,500	$2,500	$2,500	$2,500	$2,500
Net Working Capital	$0	$0	$0	($163,616)	($170,397)	($342,027)	($598,548)	($855,068)	($1,068,836)	($1,068,836)
Tax Assets	($56,859)	($421,867)	($282,917)	$154,350	$379,575	$227,717	$0	$0	$0	$0
Cash Flow From Operations	($162,453)	($1,205,333)	($808,333)	$277,384	$916,603	$1,559,665	$2,863,577	$5,093,307	$8,110,039	$11,340,539
Cash Flow From Investing	$0	$0	$0	($25,000)	$0	$0	$0	$0	$0	$0
Paid-In Capital	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Funding Need	$162,453	$1,205,333	$808,333	$0	$0	$0	$0	$0	$0	$0
Cash Flow From Financing	$162,453	$1,205,333	$808,333	$0	$0	$0	$0	$0	$0	$0
Change in Cash	$0	$0	$0	$252,384	$916,603	$1,559,665	$2,863,577	$5,093,307	$8,110,039	$11,340,539

Figure 6. Pro-forma income statement, balance sheet, and statement of cash flows.

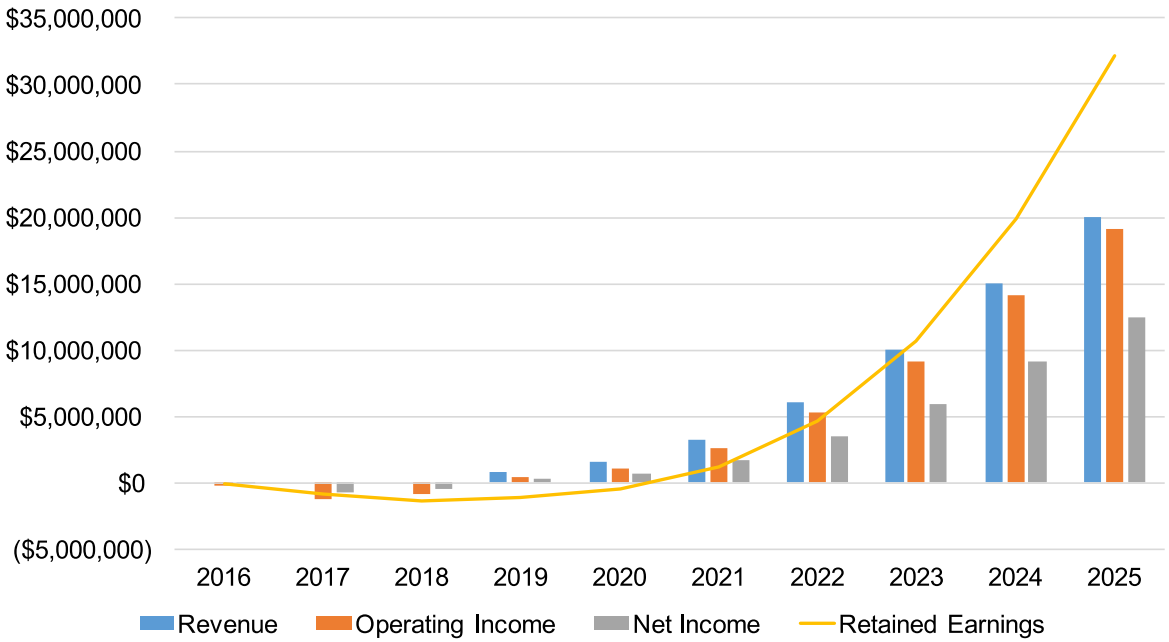


Figure 7. Pro-forma financial projections.

REFERENCES

[1] "Cancer Facts and Statistics 2015 | Research | American Cancer Society" 2015. 30 Jan. 2016 <http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2015/>

[2] American Lung Association. Lung Cancer Fact Sheet. 2016. 30 Jan. 2016 <http://www.ala1-old.pub30.convio.net/lung-disease/lung- cancer/resources/facts-figures/lung-cancer-fact-sheet.html/>

[3] Situ, BCI. "Cancer Facts & Figures 2015 - American Cancer Society." 2015. <http://www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf>

[4] Azzarelli et al. Wireless gas detection with a smartphone via rf communication. Proc. Natl. Acad. of Sci. 2014;111(51):18162-6.

[5] Methods of deposition that have been successfully employed include drawing (i.e. material abrasion), 'painting,' and ink-jet printing.

[6] Hakim et al. Volatile Organic Compounds of Lung Cancer and Possible Biochemical Pathways. Chem. Rev. 2012;112:5949-66.

[7] Toyoda Y et al. Sensitivity and specificity of lung cancer screening using chest low-dose computed tomography. Br J Cancer. 2008 May 20;98(10):1602-7.

[8] Mazzone, P Exhaled breath volatile organic compound biomarkers in lung cancer. J. Breath Res. 2012;6:027106.

[9] American Lung Association. Lung Cancer Fact Sheet.

[10] American Cancer Society. Cancer Facts and Figures, 2015.

[11] Centers for Disease Control and Prevention. National Center for Health Statistics. CDC WONDER On-line Database, compiled from Compressed Mortality File 1999-2012 Series 20 No. 2R, 2014.

[12] National Lung Screening Trial Research Team, Aberle et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395.

[13] Ma et al. Annual number of lung cancer deaths potentially avertable by screening in the United States. Cancer. 2013 Apr;119(7):1381-5.

[14] Samet JM et al. Lung cancer in never smokers: clinical epidemiology and environmental risk factors. Clin Cancer Res. 2009 sep 15;15(18):5626-5645.

[15] Glover, L. "How Much Does a CT Scan Cost?" Health. NerdWallet, 28 Oct. 2014. Web. 01 Dec. 2015.

[16] National Lung Screening Trial Research Team, Aberle et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011;365(5):395.

[17] Center for Medicare and Medicaid Services. Medicare fee schedule (outpatient radiology). 2014.

[18] Covidien. 2015 Thoracic surgery Medicare reimbursement coding guide. 2015. Covidien internal documents.

[19] Deppen et al. Cost-Effectiveness of initial diagnostic strategies for pulmonary nodules presenting to thoracic surgeons. Ann Thorac Surg. 2014 Oct;98(4):1214-22.

[20] "CT Scan vs PET Scan." Diffen.com. Diffen LLC, n.d. Web. 30 Nov 2015. <http://www.diffen.com/difference/CT_Scan_vs_PET_Scan >

[21] Moyer V on behalf of USPSTF. Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement. Med. 2014 Mar 4;160(5):330-8.

[22] Hakim et al. Volatile Organic Compounds of Lung Cancer and Possible Biochemical Pathways. Chem. Rev. 2012;112:5949-66.

[23] Song, Geng et al. "Quantitative breath analysis of volatile organic compounds of lung cancer patients." Lung Cancer 67.2 (2010): 227-231.

[24] Deng, Chunhui, Xiangmin Zhang, and Ning Li. "Investigation of volatile biomarkers in lung cancer blood using solid-phase microextraction and capillary gas chromatography–mass spectrometry." Journal of Chromatography B 808.2 (2004): 269-277.

[25] U.S. Food and Drug Administration. What are the Radiation Risks from CT? www.fda.gov, section "Radiation-Emitting Products." Updated 13 Nov 2015. Access 1 Dec 2015.

[26] Larke et al. Estimated radiation dose associated with low-dose chest CT of average-size participants in the National Lung Screening Trial. AJR Am. J. Roentgenol. 2011 Nov;197(5):1165-9.

[27] Mettler et al. Effective doses in radiology and diagnostic nuclear medicine: a catalog. Radiology. 2008 Jul;248(1):254-63.

[28] Wiener et al. Population-Based Risk for Complications After Transthoracic Needle Lung Biopsy of a Pulmonary Nodule: An Analysis of Discharge Records. Ann. Intern. Med. 2011 Aug 2;155(3):137-44.

[29] An international patent application has been filed through the MIT Technology Licensing Office.

[30]Azzarelli et al. Manuscripts in preparation.